Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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LETTER TO THE EDITOR

Takotsubo syndrome in the setting of COVID-19: Pathogenetic and diagnostic implications

Síndrome de Takotsubo no contexto da COVID-19: implicações patogénicas e diagnósticas

Takotsubo syndrome (TTS) is a form of acute cardiomyopathy primarily diagnosed via an invasive coronary angiogram (CAG) and subsequent left ventriculogram in the overwhelming majority of suspected cases.[1–3] The recently published article by Rivera K, et al. reported a TTS episode in an elderly female patient during her hospital stay for COVID-19 management.[1] Within this context, we would like to highlight further implications of TTS in the setting of COVID-19 based on this interesting case.

Firstly, severe systemic inflammation is as a well-known trigger of TTS due to a variety of proposed mechanisms, including persistent stimulation of adrenergic discharge (as a consequence of inflammation-related stress necessitating high energy consumption), adrenergic hypersensitivity (possibly mediated by cytokines) and induction of myocardial inflammation.[3] In this regard, a state of hyperinflammation (possibly together with emotional stressors including isolation and impending doom) might have contributed to the evolution of TTS in the patient.[1,3] On the other hand, cytokine release syndrome (a serious condition with high mortality that is generally encountered in frail and immunocompromised subjects with COVID-19, and is more likely to be associated with TTS evolution)[3] seems to be quite unlikely in the patient who reportedly had a favorable clinical outcome. Therefore, we wonder about other potential sources of systemic inflammation including bacterial infection, challenging medical interventions, etc. along with quantification of inflammation parameters in the patient.[1] Moreover, a variety of non-inflammatory physical stressors including severe hypoxia and associated bronchodilator therapy (particularly beta agonists in excessive amounts) might be specifically associated with TTS evolution[4] in hospitalized cases. Therefore, we also wonder about the severity of hypoxia and use of bronchodilator therapy in the patient.[1]

Of note, TTS evolution during COVID-19 appears to arise due to various combinations of inflammatory and non-inflammatory stressors[3] (with a variable contribution from each stressor in diverse clinical scenarios), potentially pointing to a specific evaluation of these stressors on a case-by-case basis. Importantly, systemic inflammation, if it emerges as the dominant stressor, may significantly worsen the clinical outcome of the associated TTS episode, due to its strong link with the evolution of malignant arrhythmogenesis, embolic events, acute respiratory distress syndrome (ARDS) as well as mechanical complications, etc.[3] Accordingly, the favorable outcome for the patient[1] potentially suggests a dominant role of non-inflammatory stressors in the evolution of her TTS episode.

Finally, we fully agree with the authors that invasive diagnostic modalities including CAG and ventriculogram could be regarded as the mandatory strategies in their case even if the findings on echocardiogram appeared to be strongly suggestive of a TTS episode.[1] As per guidelines, invasive diagnostic strategies enable visualization of patent coronary arteries and characteristic left ventriculogram in most cases with TTS (and confirm the final TTS diagnosis).[1,2] However, existing severe coronary stenosis or occlusion (suggestive of acute coronary syndromes (ACSs)) on CAG might not fully exclude a co-existing TTS episode.[2,5] Conversely, patients with characteristic findings of TTS on non-invasive imaging modalities may also suffer from co-existing ACS, thus potentially suggesting the need for invasive diagnostic modalities in these patients.[2,5] In this regard, invasive coronary imaging also allows prompt management of co-existing ACS (that might further worsen the prognosis), if any, with subsequent percutaneous coronary intervention. Importantly, the co-existence of ACSs and TTS might be even more likely in patients with certain risk factors, including severe systemic inflammation, substantial physical stressors, very old age and frailty[2,5] (as they may be consistent with the features of the reported case.[1] As expected, these risk factors may be more prevalent among COVID-19 patients. However, COVID-19 patients with a suspected TTS episode are generally less likely to undergo invasive diagnostic modalities.[1] Taken together, invasive diagnostic modalities might not only confirm the final diagnosis of TTS,[1] but might potentially uncover a co-existing ACS,[2,5] thus enabling urgent invasive management, as well. Interestingly, the clinical importance of these modalities might be even substantially higher in COVID-19 patients with a suspected TTS episode.

In conclusion, the authors[1] should be congratulated for their didactic article that might potentially serve as an epitome of TTS diagnosis and management during COVID-19.

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However, further aspects of TTS (pathogenesis, diagnostic strategies, etc.) in the setting of COVID-19 still need to be fully clarified.

Conflicts of interest

The authors have no conflicts of interest to declare.

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